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Division de la recherche

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Zeichen/Ref./Réf.	Anmeldung Nr./Application No./Demande n°.//Patent Nr./Patent No./Brevet n°
58 OL 06 30	00964659.7-2402/JP0006919

Anmelder/Applicant/Demandeur//Patentinhaber/Proprietor/Titulaire
Olympus Optical Corporation Limited

COMMUNICATION

The European Patent Office herewith transmits the Supplementary partial European search report under Rule 46(1) EPC relating to the above-mentioned European patent application.

Copies of the documents cited in the search report are enclosed.

The applicant's attention is drawn to the following:

The search Division informs the applicant that if the European search report is also to cover inventions other than the invention first mentioned in the claims, a further search fee must be paid for each of these inventions, within ONE MONTH after notification of this communication.

If the application has been filed up to 30 June 1999, the search fee in force before 01 July 1999 (EUR 869,--) or the equivalent applicable on the date of payment is payable.
This applies also to the search fees requested under Rule 46(1) EPC.
See also OJ EPO 06/1999, 405.

☐ The abstract was modified by the Search Division and the definitive text is attached to the present communication.

☑ Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.

Note to users of the automatic debiting procedure:

Unless the EPO receives prior instructions to the contrary, the search fee(s) will be debited on the last day of the period for payment. For further details see the Arrangements for the automatic debiting procedure, Supplement to OJ EPO 02/1999.

REGISTERED LETTER

European Patent Office

SUPPLEMENTARY PARTIAL EUROPEAN SEARCH REPORT

under Rule 46, paragraph 1 of the European Patent Convention

Application Number EP 00 96 4659

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Y	US 5 800 994 A (ARRUDA JOHN C ET AL) 1 September 1998 (1998-09-01) * abstract; claims 1,14-20,27-42 *	1,2,8-16	C12Q1/68 C12N9/24
Y	WO 98 04746 A (SINAI SCHOOL OF MEDICINE) 5 February 1998 (1998-02-05) * page 11, line 16 - page 13, line 28; claims 1-5; figures 1-5,7-10 *	1,2,8-16	
Y	HSUIH TERENCE CHUN ET AL: "Novel, ligation-dependent PCR assay for detection of hepatitis C virus in serum." JOURNAL OF CLINICAL MICROBIOLOGY, vol. 34, no. 3, 1996, pages 501-507, XP001097426 ISSN: 0095-1137 * page 501, column 2, last paragraph - page 502, column 2, paragraph 2; figures 1,2 *	1,2,8-16	
Y	WO 99 42614 A (LYNCH ANTHONY SIMON; SANADI ASHOK RAMESH (US); SIVARAJA MOHANRAM) 26 August 1999 (1999-08-26) * abstract; figures 1,2 *	1,2,8-16	TECHNICAL FIELDS SEARCHED (Int.Cl.7) C12Q

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LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to severalinventions or groups of inventions, namely:

see sheet B

The present partial European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims.

Place of search	Date of completion of the search	Examiner
MUNICH	21 August 2002	Stachowiak, O

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

7

EPO FORM 1503 03.82 (P04C23)

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 00 96 4659

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
Y	WO 99 35287 A (LAB OF MOLECULAR BIOPHOTONICS; ABE SATOSHI (JP); KODAMA HIROFUMI) 15 July 1999 (1999-07-15) * abstract; figures 1-5 *	1,2,8-16	
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)

EPO FORM 1503 03.82 (P04C10)

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1-2, 8-15 (completely), 16 (partially)

Methods of detecting or quantifying one or more target nucleic acids having a predetermined sequence in a specimen comprising:

(a) preparing probes A and a probe B, said probe A being a first probe which has a sequence F' complementary to a first partial sequence F of the target nucleic acid and a binding molecule bound to the sequence F', and said probe B being a second probe which has a sequence S' complementary to a second partial sequence S of the target nucleic acid and a flag bound to the sequence S', where said flag is a double-stranded sequence and has a marker substance in one of the double strand; (b) hybridizing the first probe A with the first partial sequence F of the target nucleic acid and hybridizing the second probe B with the second partial sequence S of the target nucleic acid;
(c) ligating the first probe A and the second probe B both being hybridized with the target nucleic acid, thereby obtaining a probe (A+B);(d) binding the binding molecule to a substance capable of being paired up therewith, thereby recovering the probe (A+B); and (e) recovering a single-stranded nucleic acid having the marker substance of the double stranded nucleic acid constituting the flag and detecting or quantifying the marker substance or the dissociated single stranded sequence from the flag, thereby detecting or quantifying the target nucleic acid in the specimen.

2. Claims: 3-4 (completely), 16 (partially)

Methods of detecting or quantifying one or more target nucleic acids having a predetermined sequence, in a specimen, comprising:
(a) preparing a probe A and a probe B, said probe A being a first probe which has a sequence F' complementary to a first partial sequence F of the target nucleic acid and a tag sequence Tg bound to the sequence F', and said probe B being a second probe which has a sequence S' complementary to a second partial sequence S of the target nucleic acid and a marker substance bound to the sequence S'
(b) mixing the probe A, the probe B, and the specimen, thereby hybridizing the probe A with the first partial sequence F of the target nucleic acid and simultaneously hybridizing the probe B with the second partial sequence S of the target nucleic acid;
(c) ligating the probe A and the probe B, both being hybridized with the target nucleic acid, thereby obtaining a probe (A+B);
(d) dissociating the probe (A+B) from the target nucleic

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

acid;
(e) hybridizing the tag sequence Tg with a sequence Tg' complementary to the tag sequence Tg, thereby recovering the probe (A+B); and
(f) detecting or quantifying the marker substance in the probe (A+B) recovered, thereby detecting or quantifying the target nucleic acid in the specimen.

3. Claims: 5-7 (completely), 16 (partially)

Methods of detecting or quantifying one or more target nucleic acids having a predetermined sequence in a specimen, comprising:
(a) preparing a probe A and a probe B, said probe A being a first probe which has a sequence F' complementary to a first partial sequence F of the target nucleic acid and a tag sequence Tg bound to the sequence F', and said probe B being a second probe which has a sequence S' complementary to a second partial sequence S of the target nucleic acid, a flag sequence FL bound to the sequence S', and a marker substance bound to the flag sequence FL;
(b) mixing the probe A, the probe B, and the specimen, thereby hybridizing the probe A with the first partial sequence F of the target nucleic acid and simultaneously hybridizing the probe B with the second partial sequence S of the target nucleic acid;
(c) ligating the probe A and the probe B, both being hybridized with the target nucleic acid, thereby obtaining a probe (A+B);
(d) dissociating the probe (A+B) from the target nucleic acid;
(e) hybridizing the tag sequence Tg contained in the probe (A+B) with a sequence Tg' complementary to the tag sequence Tg, thereby dissociating the probe (A+B); and
(f) recovering a portion containing at least the probe B from the prove (A+B) hybridized with the sequence Tg';
(g) hybridizing the flag sequence FL recovered with a nucleic acid sequence FL' complementary to the flag sequence FL, thereby specifically recovering the portion containing at least probe B; and
(h) selectively detecting the marker substance contained in the portion containing at least the probe B recovered, thereby detecting or quantifying the target nucleic acid in the specimen.

The above-mentioned 3 groups of claims lack unity a posteriori because their common inventive concept is known from the prior art, i.e., no special technical feature or corresponding technical feature linking the above-mentioned groups of claims exists. This is because the features the above groups of claims have in common are i) the hybridisation of two incomplete probes to a target nucleic acid ii) ligation of these

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probes and iii) subsequent capture of the probes and detection of the label (or labelled nucleic acid strand).

However, nucleic acid detection and quantification methods sharing the above-mentioned common inventive principle are already known from e.g. US 5,800,994 (Martinelli et al.), and WO98/04746 (Zhang et al.). US 5,800,994 discloses a method employing two partial probes which are hybridised to a target nucleic acid strand and are subsequently ligated. After denaturation, the ligated probe is captured and detected by its label moiety (cf. Martinelli et al. claims 1, 14). Also, Zhang et al. discloses the latter general principle (cf. e.g. Zhang et al., Figure 1) which renders the above mentioned groups of claims non-unitarian.

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 00 96 4659

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

21-08-2002

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		AU 684915 B2	08-01-1998
		AU 1958595 A	23-10-1995
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WO 9942614 A	26-08-1999	US 6153384 A	28-11-2000
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WO 9935287 A	15-07-1999	EP 1016731 A1	05-07-2000
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